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Concepts of herd protection and immunity

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Abstract

Vaccines are designed primarily to protect vaccinated individuals against the target infection. In addition to this direct effect of vaccination, vaccination may increase the level of population (or herd) immunity by increasing the proportion of the population who are immune from infection. For infections that are transmitted from person-to-person, or for which humans are important reservoirs of the infectious agent, an increase in the level of herd immunity may result in a lower force of infection in the population and thus a lower risk of infection among unvaccinated persons. This is called an indirect effect of vaccination, or a herd-protective effect. The effect of vaccination in increasing the level of herd immunity is important in disease elimination programmes as, because of the indirect effect of vaccination on risk of infection, elimination may be achieved without having to vaccinate the entire population. An example is given of how the indirect effect of vaccination operates and the implications that this has for both disease control programmes and the interpretation of vaccine trials are discussed

Keywords: Herd immunity, herd effects, basic reproductive number, effective reproductive number, indirect protection, infection elimination

1. Introduction

For many infectious agents, the number of individuals in a population (herd) who are (relatively) immune to infection with an infectious agent depends on the proportion who have previously been infected with the infectious agent and the proportion of the remainder who have been immunised with an efficacious vaccine against the agent. A measure of the level of population-immunity, or herd-immunity, is the proportion who are thus immune from further infection. For many infections, the level of herd immunity in a population may have an effect on the amount of transmission of the infection within the population and, in particular, may affect the risk of an uninfected becoming infected. For such infections, increasing the level of herd immunity will decrease the risk of an uninfected person becoming infected [1-3].

For some infections this so-called herd effect, or herd protection, may be very important for disease control through vaccination. If the herd effect reduces the risk of infection among the uninfected sufficiently, then the infection may no longer be sustainable within the population and the infection may be eliminated. This concept is important in disease elimination or eradication programmes. It means, for example, that elimination of the infectious agent in a population can be achieved without necessarily vaccinating the entire population.

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Infections for which herd immunity may be important in affecting the risk of infection among non-immunes in the population are those infections which are transmitted directly from person to person (e.g. measles, rubella, varicella) or for which humans are the reservoir, or an important reservoir, of infection (e.g. polio, malaria). There may be no herd protection the infection is not generally transmitted from person to person and if humans are not an important reservoir of infection (e.g. tetanus, rabies).

2. Infection in naïve populations and the basic reproduction number (R_0)

Imagine a situation in which a person acquires an infection and then migrates to a population in which the infectious agent has never previously circulated, and thus all in the population are susceptible to infection. While the person is infectious and is capable of transmitting the infectious agent to others, he or she will have contact with a number of other persons that is sufficiently "close" to infect them. The number of persons thus infected will depend upon multiple factors, including the nature of the infectious agent and the contact patterns of the infectious person. However, it is possible to conceive of the average number of new transmissions of an infectious agent that will typically occur directly from an infectious person when he or she is newly introduced into the totally susceptible population. This average number is known as the ***basic reproductive number*** and is commonly designated symbolically as "$\mathbf{R_0}$" - the average number of other persons that an infectious person will infect with an agent in a completely susceptible population.

R_0 will vary between different infectious agents depending on the infectiousness of the agent, which is influenced by factors such as: how long it survives in the environment; the dose necessary for infection; the duration of infectiousness in the host, and whether or not infectiousness precedes infection symptoms. R_0 may also vary from population to population depending on factors such as population density, which may affect the number of effective contacts a person has while he/she is infectious. It may also vary with season for some infections, as the ambient conditions may affect the survival of the agent in the environment and the extent to which people have close contact with each other may be different in warmer and colder periods.

3. Infection in populations in which some are immune: indirect protection and the effective reproduction number (R)

The indirect protection that may be provided to unvaccinated persons if the level of herd immunity is increased by vaccination is illustrated schematically in **Figure 1**. We consider an "idealised" population in which during the period of infectiousness an infectious person has contact with 4 other persons and with 2 of the 4 the contact is "close" enough for the infection to be transmitted.

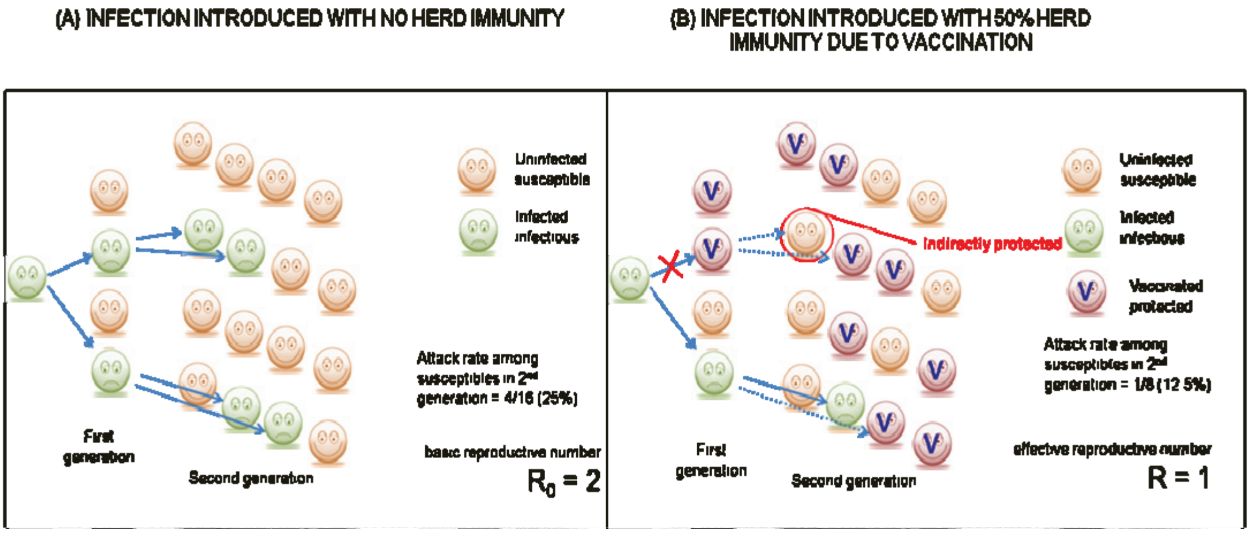

Figure 1: Idealised example illustrating the indirect protective effect of vaccination (herd-effect) when 50% of a naïve population is rendered immune by vaccination

Thus in **Figure 1**(A), when the infectious person is introduced into a totally susceptible population, he or she infects 2 others (first generation) and then these 2 others each go on to infect a further 2 others of their 4 contacts (second generation). In this situation the basic reproductive number (R_0) is 2.

Now consider the same situation after half of the population has been rendered immune to infection by vaccination, so that (on average) 2 out each person's 4 contacts will be not-susceptible to infection. When the initial infectious person is introduced into the population only one infection results (first generation) as one of the contacts who previously would have been infected has been protected by vaccination. Similarly, the 1 newly infected person only goes on to infect 1 person (second generation) because half of the contacts have been directly protected by vaccination. In this situation the *effective reproductive number* (sometimes designated by "R") is thus 1.

Note the person circled in **Figure 1**(B). This person was infected in the scenario considered in **Figure 1(A)** but was not infected in the scenario considered in **Figure 1(B)**, even though the person had not been vaccinated. This is because the person was indirectly protected, as the person who would have infected them was themselves protected by vaccination and therefore did not pass the infection on. This is an illustration of a herd-protective effect of vaccination, where increasing the level of vaccination (in this case from zero to 50%) has reduced the risk of infection among the unvaccinated. Thus, in scenario (A) the attack rate among susceptibles in the second generation was 25% whereas in scenario (B) it is 12.5%

4. The herd immunity threshold

In order for an infection which is transmitted from person to person, or for which humans are the principal reservoir, to be maintained in a population, each case of infection must give rise to at least one other case – i.e. the effective reproduction number must be above 1. If the effective reproduction number is below 1 then the infection will eventually die out in the population. That is, if the herd protective effect reduces the risk of infection among the uninfected sufficiently, then the infection will no longer be sustainable within the population and the infection will be eliminated.

In general, the effective reproductive number (R) will be lower than the basic reproductive number (R_0), depending on the proportion (P) of the population who are immune to infection. Such immunity may be induced either by a previous infection with the agent (if such infection produced immunity) and/or by immunisation with an effective vaccine. Simply, $R = (1-P) * R_0$.

Therefore, for infection elimination or eradication – i.e. to reduce R below 1, then P must be equal to at least $(1-1/R_0)$. So, for example, if $R_0 = 5$ then P must be at least $(1-1/5) = 0.8$. That is, 80% of the population must be immune, either through previous infection or vaccination.

The value of P that reduces R to at most 1 is commonly called the "herd immunity threshold" – the level of population immunity that is necessary for the infection to be no longer self-sustaining in the population.

Table 1 shows estimated values of R_0 for some common infections and the derived values for the herd immunity thresholds using the formula given above. The higher the value of R_0 the higher the level of population immunity required (often achieved by increasing population coverage with a vaccine against the agent) for disease elimination. The estimated value of R_0 for pandemic

Table 1. Herd Immunity Thresholds (Approximate) for Infection Elimination

Infection	R_0	Herd immunity threshold
Diphtheria	6-7	85%
Measles	12-18	83-94%
Mumps	4-7	75-86%
Pertussis	12-17	92-94%
Polio	5-7	80-86%
Rubella	6-7	83-85%
Smallpox	5-7	80-85%
Pandemic influenza (H1N1)	1.6?	~40%

Taken, in part, from Fine[3][3]

influenza has varied in different studies but, usually, it appears to be low compared with other common infections and past pandemic influenza viruses. If it is as low as 1.6, as indicated in **Table 1**, then once about 50% of a population have been infected or vaccinated the infection may no longer show epidemic characteristics and will not be sustained in the population. It is important to stress that R_0 may vary between different populations and in different segments, or at different times, in the same population, as discussed above. Thus the required herd immunity threshold for infection elimination may be more complex to estimate that the simple formula given above.

5. Infection elimination and eradication

In common English the terms "elimination" and "eradication" are used interchangeably. However, in the parlance of disease control programmes they have come to have distinct definitions, as given below [4]:

Elimination of infections: Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent re-establishment of transmission are required. Example: measles, poliomyelitis.

Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed. Example: smallpox.

6. Beneficial and deleterious effects of herd protection

A major beneficial effect of increasing the level of population immunity through vaccination is that it may result in the elimination of the infectious agent from the population. Even if the increase in population immunity is not sufficient to achieve infection elimination (because, for example, the efficacy of the vaccine is poor or it is not possible to achieve sufficiently high vaccine coverage), the risk of infection among unvaccinated person may still be reduced. This may be particularly important for those for whom vaccination is contraindicated (e.g. some live vaccines are not recommended for persons who are immunosuppressed). Also discussed in this context is the so-called "free-rider" paradox – that is, the "optimal" strategy for an individual with respect to vaccination in a population is that everybody else is vaccinated and the individual is not! Thus, the individual is protected from infection because of the herd effect, but suffers none of the potential adverse effects of vaccination (which are observed for all vaccines, albeit at a very low level for most).

Although reducing the risk of infection among susceptible is generally a benefit, for some infections it may also result in deleterious effects. For example, for common childhood infections, a consequence of reducing the risk of infection among susceptible is that for those who are infected the average age at infection will increase. This may be of consequence when the clinical consequences of infection are greater for those infected at older ages (e.g. polio, rubella, varicella, measles, and hepatitis A).

7. Measurement of direct and indirect effects of vaccination in controlled trials

As discussed above, the indirect protective effect of a vaccine increases protection against infection even among the unvaccinated. Thus, the overall reduction in the incidence of infection in a population is greater than that which would be predicted just based on the direct protection that the vaccine gives to a vaccinated person. Controlled trials that are conducted before licensure of a vaccine are generally designed to measure the individual protective effect of a vaccine whereas herd effects are evaluated once the vaccine has been introduced into public health programmes. The rationale for basing licensure of a vaccine on the individual protective effect is based on several considerations. First, demonstration of individual protection is critical, as only if the vaccine can be demonstrated to protect the individual will there be any possible herd effect. Secondly, the individual protective effect of a vaccine is likely to be a property that is relatively invariant to the population in which the vaccine is being evaluated [1], whereas the indirect effects of a vaccine will vary according to vaccine coverage in a population and may also vary from population to population, depending on the epidemiology of the infection in different environments. Thirdly, in general, it is necessary to vaccinate larger numbers of people to demonstrate a herd effect compared to the number required to establish individual protection, and some argue it is unethical to expose larger numbers of volunteers to an unlicensed product before individual protection is established.

Nonetheless, for some vaccines the decision whether to use a licensed product in a public health programme may depend upon the magnitude of the herd effect, particularly if the vaccine is expensive. Therefore, at some point, before or after licensure, studies to measure the magnitude of any herd effects may become a priority. Such studies may be conducted after a vaccine has been introduced into a public health programme, and these are generally observational studies from which bias may be difficult to eliminate completely. The possibility of conducting cluster randomised trials to evaluate both individual and herd protective effects has been advocated [5,6]. One possibility would be to randomise communities to either vaccine or control arms and the differences in the incidence of infection in vaccinated and unvaccinated communities would give a measure of the overall protective effect of vaccination, incorporating the summation of both direct and indirect effects.

Another alternative, illustrated in **Figure 2**, would be to allocate some communities to receive no vaccine (control communities – Population 2 in **Figure 2**) and to randomise a proportion, say a half, of individuals in other communities to receive vaccine (Population 1 in **Figure 2**). By comparing the incidence of infection in different groups of persons, measures of both direct and indirect effects can be obtained. First the *direct protective effect* of vaccination is obtained by comparing the incidence of infection among vaccinated and unvaccinated persons in Population 1: this is essentially the classic individually randomised controlled trial. A measure of the *indirect protective effect* of vaccination can be obtained by comparing the incidence of infection among unvaccinated persons in Population 1 and those in Population 2, all of whom are unvaccinated. A measure of the *overall protective effect of vaccination* (combining both direct and direct effects) is obtained by comparing the incidence of infection among all persons in Population 1 with the incidence of infection among all persons in Population 2.

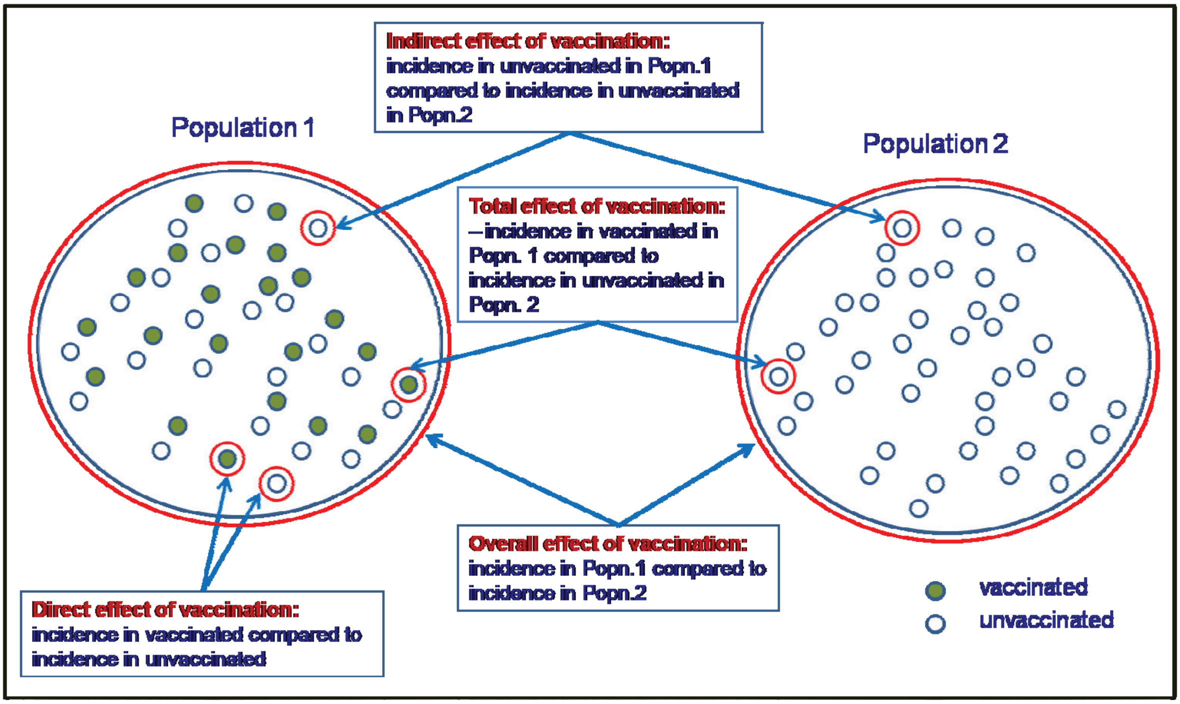

Figure 2: Measurement of direct and indirect effects of vaccination

Any herd effect of vaccination in Population 1 reduces the risk of infection of both vaccinated and unvaccinated persons in that population. Thus, a measure of what has been called the *total protective effect* of vaccination [6] among the vaccinated is provided by comparing the incidence of infection among the vaccinated in Population 1 with the incidence of infection among all those (unvaccinated) in Population 2.

Trials of this kind would be valuable to establish whether or not there was evidence of herd protective effects and to document the magnitude of these effects in a particular situation (in the example, with 50% vaccine coverage), but it is important to note that the magnitude of any herd effects is influenced critically by the proportion of the population that has been vaccinated. Thus it may be difficult to generalise from a trial of the kind outlined in estimating the magnitude of the herd protective effects when a vaccine is introduced in a public health programme.

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